[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH]

Preparation and Properties of 3,5-Di-O-benzoyl-1,2-O-(1-hydroxybenzylidene)-α-D-ribose, an Orthobenzoic Acid Derivative of D-Ribofuranose

BY ROBERT K. NESS AND HEWITT G. FLETCHER, JR.

RECEIVED NOVEMBER 9, 1953

The hydrolysis of tri-O-benzoyl-β-D-ribofuranosyl bromide gives the previously reported 2,3,5-tri-O-benzoyl-β-D-ribose together with a new, crystalline isomer. The latter, which is stable to dilute acid, is readily isomerized by aqueous pyridine to the former. Synthesis of the new isomer through hydrogenolysis of amorphous 3,5-di-O-benzoyl-1,2-O-(1-benzyloxybenzylidene)-α-D-ribose indicates that it is most probably 3,5-di-O-benzoyl-1,2-O-(1-hydroxybenzylidene)-α-D-ribose, an orthobenzoic acid derivative. Treatment of the new substance with hydrogen bromide affords a crystalline, highly reactive 3,5-di-O-benzoyl-D-ribofuranosyl bromide which, on hydrolysis, gives amorphous 3,5-di-O-benzoyl-D-ribose. Successive oxidation, reduction, deacylation and benzoylation of the latter leads to erythritol tetrabenzoate. Treatment of either the new isomer or the crystalline bromide with zinc chloride in acetic anhydride gives a crystalline 1,2-di-O-acetyl-3,5-di-O-benzoyl-D-ribose. With hydrogen bromide this latter compound gives an amorphous bromide which, on hydrolysis, yields a crystalline substance which appears to be 3,5-di-O-benzoyl-1,2-O-(1-hydroxyethylidene)-α-D-ribose, an orthoacetic acid derivative. Ortho acid derivatives, a relatively rare type of substance, are briefly discussed.

The preparation of crystalline 2,3,5-tri-O-benzoyl-β-D-ribose in relatively high yield from D-ribose without the isolation of crystalline intermediates has been described in a recent paper.[1] In this process D-ribose is converted into a mixture of methyl D-ribofuranosides which is benzoylated and then treated with hydrogen bromide in glacial acetic acid. The crude tri-O-benzoyl-β-D-ribofuranosyl bromide (I) thus formed is hydrolyzed in aqueous acetone and the product crystallized from aqueous pyridine as 2,3,5-tri-O-benzoyl-β-D-ribose (IV) containing pyridine of crystallization. When, however, the product is not subjected to the action of pyridine or other base the 2,3,5-tri-O-benzoyl-β-D-ribose (IV) is accompanied by a wholly different crystalline substance which is obtained in 43% yield. The latter compound may be obtained in slightly better yield by the hydrolysis of the purer but yet amorphous tri-O-benzoyl-β-D-ribofuranosyl bromide (I) which may conveniently be prepared from 2,3,5-tri-O-benzoyl-β-D-ribose (IV).[1] The new substance has the composition of a tribenzoylpentose but, in contrast to the 2,3,5-tri-O-benzoyl-β-D-ribose previously reported (anhydrous form: m.p. 111–112°, $[\alpha]^{20}\text{D}$ +67.7° → +65.6° ($CHCl_3$, 2 days)),[2] it melts at 142–143° and rotates +85.3° in chloroform.[3] The new benzoate does not mutarotate in aqueous dioxane even when a trace of hydrogen bromide is added. The presence of ammonia or pyridine causes a rapid mutarotation, however, to the specific rotation of 2,3,5-tri-O-benzoyl-β-D-ribose (IV) and this latter compound can then be isolated in good yield. The failure of the new isomer to mutarotate in acid solution appeared to eliminate the possibility that it was simply the anomer of the known 2,3,5-tri-O-benzoyl-β-D-ribose. The only other likely structural isomer is that of the orthobenzoic acid derivative II which may be given the formal name 3,5-di-O-benzoyl-1,2-O-(1-hydroxybenzylidene)-α-D-ribose.[4] To test whether structure II might represent the new isomer, tri-O-benzoyl-β-D-ribofuranosyl bromide (I) was condensed with benzyl alcohol in the presence of quinoline, an acid acceptor which has been found to favor the formation of ortho glycosides from *trans*-halides.[5–7] The desired product, 3,5-di-O-benzoyl-1,2-O-(1-benzyloxybenzylidene)-α-D-ribose (III), was obtained only in amorphous form, but its nature as an ortho glycoside was confirmed by the fact that it mutarotated rapidly to the left in benzyl alcohol solution when a trace of acid was added—behavior typical of an ortho glycoside of the α-D-series.[8] It is to be expected that the sirupy material was contaminated with the two anomeric benzyl D-ribofuranoside tribenzoates. Hydrogenolytic removal of the benzyl group in the crude amorphous ortho glycoside III led to the isolation of the new D-ribose tribenzoate in 21% yield and of 2,3,5-tri-O-benzoyl-β-D-ribose (IV) in 52% yield, neutral media being used throughout. Since hydrogenolysis of the benzyl group in the ortho glycoside should disturb neither ring structure nor asymmetric center, this synthesis lends support to the view that the new tribenzoate is II.

When a 2,3,4- or a 2,3,5-tri-O-benzoylpentose (such as IV) is dissolved in methylene chloride and gaseous hydrogen bromide is passed into the solution a turbidity is formed almost immediately due to the water produced by the replacement of the hydroxyl at carbon 1 with bromine. The behavior of the new D-ribose tribenzoate under these conditions is quite different: the solution remains clear and is found to contain benzoic acid. Concentration yields a very reactive crystalline bromide which, from analytical values, appears to be a di-O-benzoylpentosyl bromide VII. The ease with which the bromine is hydrolyzed indicates that it is

---

(1) R. K. Ness, H. W. Diehl and H. G. Fletcher, Jr., THIS JOURNAL, **76**, 763 (1954).

(2) Melting points cited are corrected. Unless otherwise stated rotations are specific rotations for the D line of sodium at 20°, concentration being expressed in g. per 100 ml. of solution.

(3) These constants agree quite closely with those reported by F. Weygand and F. Wirth [*Chem. Ber.*, **85**, 1000 (1952)] for a substance which they obtained through the hydrolysis of amorphous triobenzoyl-D-ribofuranosyl bromide as well as through the acid hydrolysis of a partially benzoylated adenosine and designated as 2,3,5-tri-O-benzoyl-D-ribose. ADDED IN PROOF FEBRUARY 5, 1954.—A comparison of the two substances, kindly undertaken by Prof. Weygand, has shown them to be identical.

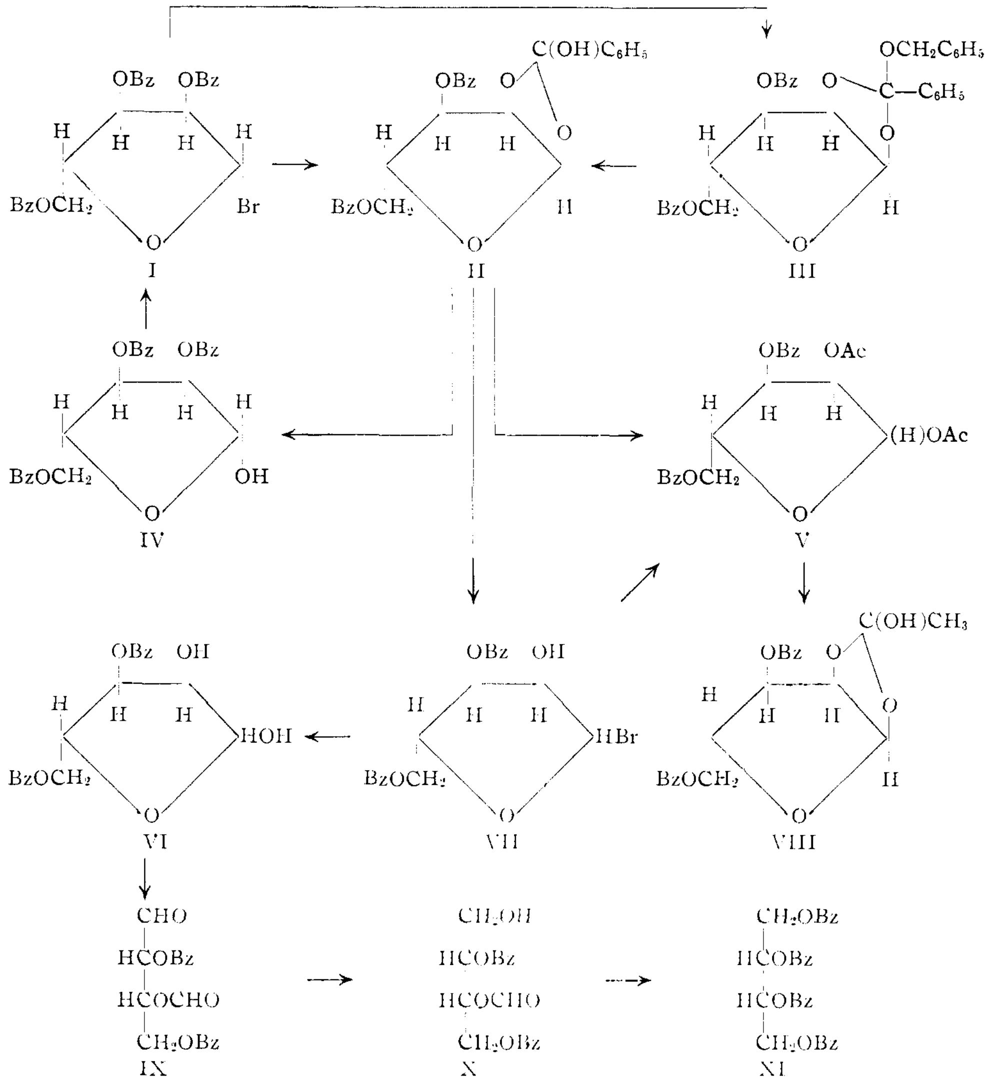
(4) The nomenclature employed in this paper follows the Rules of Carbohydrate Nomenclature which were approved by the Council of the American Chemical Society and were published in *Chem. Eng. News*, **31**, 1776 (1953).

(5) E. Fischer, M. Bergmann and A. Rabe, *Ber.*, **53**, 2362 (1920).

(6) H. G. Bott, W. N. Haworth and E. L. Hirst, *J. Chem. Soc.*, 1395 (1930).

(7) E. Pacsu, *Advances in Carbohydrate Chem.*, **1**, 77 (1945).

(8) *Cf.* R. K. Ness, H. G. Fletcher, Jr. and C. S. Hudson, THIS JOURNAL, **73**, 296 (1951), who describe the behavior of a methyl ortho glycoside of the β-L-series in acidic methanol.



attached at carbon 1. To locate the unacylated position the bromide was hydrolyzed to give a sirup, presumably VI, which was found to consume but 0.78 mole of lead tetraacetate. Surprisingly, no formic acid was detected in this oxidation; it may have been bound quite firmly to the oxidation product as a secondary formyl ester IX. In any case, the product from the oxidation of VI with lead tetraacetate was reduced catalytically (to X?), deacylated and then benzoylated to give erythritol tetrabenzoate (XI). The isolation of an erythritol derivative after this sequence of reactions indicates that the hydroxyl group on carbon 2 in VII is unsubstituted. It seems likely, then, that the first step in the action of hydrogen bromide on the orthobenzoic acid II is to form 1,3,5-tri-*O*-benzoyl-D-ribose which then, in normal fashion, gains a bromine at carbon 1 in place of a benzoyloxy group.

Both acetylation and benzoylation of the new tribenzoate II in pyridine solution afforded dextrorotatory products from which no crystalline material was obtained.[9] When, instead of pyridine, an acidic catalyst, zinc chloride, was used with acetic anhydride a readily crystalline diacetyldibenzoylpentose was obtained. That the substance was 1,2-di-*O*-acetyl-3,5-di-*O*-benzoyl-D-ribose (V) appeared likely from the fact that it could equally well be obtained through a similar acetylation of 3,5-di-*O*-benzoyl-D-ribofuranosyl bromide. It is suggested that the first step in the acidic acetylation of II produces 2-*O*-acetyl-1,3,5-tri-*O*-benzoyl-D-ribose and the benzoyl attached to carbon 1 is then replaced by acetyl to give V. That such replacements at carbon 1 are readily accomplished under these conditions was shown by converting β-D-ribofuranose tetrabenzoate[1] into 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-D-ribose through the action of zinc chloride in acetic anhydride.

The diacetate V led us to another interesting derivative. When it was treated with hydrogen bromide and the resultant product hydrolyzed, a crystalline monoacetyldibenzoyl-D-ribose was ob-

---

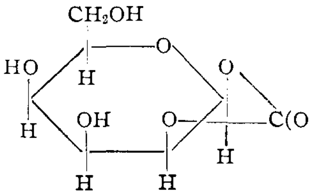
(9) These experiments were carried out before the rapid mutarotation of the tribenzoate in pyridine had been observed; although the solid tribenzoate was added to chilled acylating mixtures, doubtless some of the material was at least in process of rearrangement when it was acylated and it is not surprising that the resulting mixture proved refractory. Weygand and Wirth (ref. 3) have obtained 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribose and β-D-ribofuranose tetrabenzoate from II; evidently rearrangement preceded acylation in these cases.

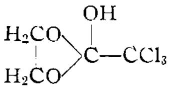
tained. The same substance could be obtained directly from the orthobenzoic acid II by hydrolysis of the product obtained through the action of hydrogen bromide in a mixture of glacial acetic acid and acetic anhydride. Since polarimetric studies showed the monoacetate to be markedly more labile in the presence of pyridine than of hydrobromic acid it is tentatively assigned the structure VIII, the acetic acid analog of II. Of course, in neither case is it possible as yet to assign a configuration to the asymmetric carbon of the acid radical.[10]

It might be predicted that 2,3,5-tri-*O*-benzoyl-β-D-ribose (IV) with its three ester carbonyl groups would show an absorption peak in the ultraviolet region about 50% greater than 3,5-di-*O*-benzoyl-1,2-*O*-(1-hydroxybenzylidene)-α-D-ribose (II) with its two ester carbonyl groups. Actually IV and II in absolute ethanol solution showed molecular extinction coefficients at 230 mμ of 42,000 and 38,600, respectively.

Discussion

Pacsu[7] and Pigman and Isbell[11] have reviewed the relatively few substances which, on the basis of the indirect evidence afforded by their properties, have been assigned cyclic orthoacid structures (2-hydroxy-1,3-dioxolanes) analogous to II. Most interesting among these from the present point of view is the D-talose monobenzoate which Pigman and Isbell[11] obtained as a by-product in the oxidation of D-galactal by perbenzoic acid. Like the orthobenzoic acid (II) described in the present paper this compound was stable in dilute acid and mutarotated in the presence of base. These properties, unlike those of a 1- or 2-*O*-benzoylaldose, as well as the method of preparation led these authors to suggest that their monobenzoate was 1,2-*O*-(1-hydroxybenzylidene)-β-D-talose (XII). Although Meerwein and his co-workers[12-14] have reported that 2-trichloromethyl-2-hydroxy-1,3-dioxolane (XIII) reacts with diazomethane to give a methyl ether, neither the talose monobenzoate of Pigman and Isbell nor the 3,5-di-*O*-benzoyl-1,2-*O*-(1-hydroxybenzylidene)-α-D-ribose (II) described in the present paper was found to react with diazomethane. The reason for this difference may possibly be that the presence of the three chlorine atoms in XIII tends to make the adjacent hydroxyl group more acidic than those in II and XII.


XII


XIII

In previous papers[15,16] from this Laboratory the neighboring group theory of Winstein[17] has been successfully invoked to rationalize a number of reactions of the benzoylated glycopyranosyl halides. On the basis of this experience it seems reasonable to assume, therefore, that a halide which gives II on hydrolysis with water and III on treatment with benzyl alcohol and an acid acceptor must be the *trans*-halide I, tri-*O*-benzoyl-β-D-ribofuranosyl bromide.[18] The actual substance, however, has not been obtained in crystalline form and may, like its pyranose analog,[16] be contaminated with the anomeric halide.

It is natural to ask why ortho acids like II have not been encountered more frequently in the sugar series as the products of the hydrolysis of *trans*-acyloglycosyl halides. Two reasons may be advanced to explain this. First, the ortho acids are in general relatively labile substances, and, second, attention has been largely directed to the hydrolysis of pyranosyl rather than furanosyl halides. In the favored pyranose conformations[19] *cis* substituents at carbons 1 and 2 are not in such close juxtaposition as they are in the more nearly planar furanose derivatives. From models it is evident that such *cis* substituents must be close together in order to take part in the formation of the planar 1,3-dioxolane ring.

Our studies on the carbohydrate ortho acids are continuing with the hope that we may be able to throw more light upon this interesting group of substances.

Experimental

3,5-Di-*O*-benzoyl-1,2-*O*-(1-hydroxybenzylidene)-α-D-ribose (II). (a) From 2,3,5-Tri-*O*-benzoyl-β-D-ribose (IV).—A solution of 10.11 g. of 2,3,5-tri-*O*-benzoyl-β-D-ribose[1] in a mixture of 30 ml. of methylene chloride and 3.5 ml. of acetic anhydride was treated with 10 ml. of a solution of hydrogen bromide in glacial acetic acid (*ca.* 32% HBr). After six minutes at 20° the reaction mixture was poured into a mixture of ice-water and methylene chloride. The organic layer was quickly washed with cold sodium bicarbonate solution, dried with sodium sulfate, filtered through decolorizing carbon and, finally, concentrated *in vacuo* (35° bath) to a frothy mass. The crude bromide thus obtained was dissolved in a mixture of 40 ml. of acetone and 2 ml. of water. After 75 minutes at room temperature, methylene chloride was added and the mixture washed with cold sodium bicarbonate solution. Moisture was removed with sodium sulfate and the solution concentrated *in vacuo* (30° bath) to a semi-crystalline residue to which 70 ml. of ether and then 35 ml. of pentane were added. Practically pure 3,5-di-*O*-benzoyl-1,2-*O*-(1-hydroxybenzylidene)-α-D-ribose (5.10 g., 50%) melting at 142–143° and rotating +86° in chloroform (*c* 0.93) was thus obtained. Recrystallization from a mixture of 10 parts of acetone and 5 parts of water afforded fine needles melting at 142–143° and rotating +85.3° in chloroform (*c* 0.97).

Anal. Calcd. for $C_{26}H_{22}O_8$: C, 67.52; H, 4.80. Found: C, 67.47; H, 4.88.

---

[10] Structures V to VIII have been formulated as D-ribose derivatives. Although there is no proof at present that carbon 2 in these substances is actually a D-carbon it seems somewhat unlikely that inversion of configuration has taken place in the course of the reactions used to prepare these compounds from II.

[11] W. W. Pigman and H. S. Isbell, *J. Research Natl. Bur. Standards*, **19**, 189 (1937).

[12] H. Meerwein and G. Hinz, *Ann.*, **484**, 1 (1930).

[13] H. Meerwein and H. Sönke, *Ber.*, **64**, 2375 (1931).

[14] H. Meerwein and H. Sönke, *J. prakt. Chem.*, **137**, 295 (1933).

[15] R. K. Ness and H. G. Fletcher, Jr., THIS JOURNAL, **75**, 2619 (1953), and references cited therein, especially ref. 16 cited below.

[16] R. K. Ness, H. G. Fletcher, Jr., and C. S. Hudson, *ibid.*, **73**, 959 (1951).

[17] S. Winstein and R. E. Buckles, *ibid.*, **64**, 2780 (1942); S. Winstein, H. V. Hess and R. E. Buckles, *ibid.*, **64**, 2796 (1942); A. E. Remick, "Electronic Interpretations of Organic Chemistry," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1949, p. 339.

[18] The fact that Weygand and Wirth (ref. 3) have obtained II through the acid hydrolysis of a partially benzoylated adenosine may similarly be regarded as a confirmation of the β-configuration of the D-ribofuranose residue in this nucleoside.

[19] R. E. Reeves, THIS JOURNAL, **72**, 1499 (1950).

The mother liquor from the above preparation was concentrated to a sirup which, from ether–pentane, afforded crude crystalline 2,3,5-tri-*O*-benzoyl-β-D-ribose in 32% yield.

(b) **From D-Ribose.**—Five grams of pure D-ribose was converted successively to methyl D-ribofuranoside, methyl D-ribofuranoside tribenzoate and 2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl bromide as described for the preparation of 2,3,5-tri-*O*-benzoyl-β-D-ribose in an earlier paper.[1] The amorphous bromide was dissolved in a mixture of 60 ml. of acetone and 3 ml. of water and, after 40 minutes at room temperature, the solution was diluted with methylene chloride and washed with cold aqueous sodium bicarbonate solution. Moisture was removed with sodium sulfate and the solution concentrated *in vacuo* to give a sirup which, from a mixture of 120 ml. of ether and 60 ml. of pentane, gave 6.55 g. (43%) of 3,5-di-*O*-benzoyl-1,2-*O*-(1-hydroxybenzylidene)-α-D-ribose melting at 141–142°. Solvent was removed from the mother liquor and the resulting sirup dissolved in a mixture of 60 ml. of pyridine and 37 ml. of water. At −5° there was obtained 2,3,5-tri-*O*-benzoyl-β-D-ribose as its crystalline addition compound with pyridine. Dried *in vacuo* over sulfuric acid, the solvent-free product weighed 5.4 g., raising the total yield of pentose tribenzoates to 78%.

(c) **From Amorphous 3,5-Di-*O*-benzoyl-1,2-*O*-(1-benzyloxybenzylidene)-α-D-ribose (III).**—A cold solution of 5.00 g. of 2,3,5-tri-*O*-benzoyl-β-D-ribose in 25 ml. of ethylene chloride over solid Drierite was nearly saturated with gaseous hydrogen bromide, the Drierite removing the water formed in the reaction. After 65 minutes at 0° the mixture was filtered and concentrated *in vacuo* at room temperature. The thick sirup thus obtained was dissolved in 10 ml. of ethylene chloride and 5 ml. of quinoline added. After cooling, the solution was treated with 2.5 ml. of benzyl alcohol and left at 0–5° for 19 hours. The reaction mixture was then diluted with methylene chloride, poured on ice, and the organic layer washed, first with cold 3 *N* sulfuric acid, and then with aqueous sodium bicarbonate. After drying with sodium sulfate the solution was concentrated *in vacuo* to give a sirup (6.5 g.). A sample of this sirup rotated +81° in benzyl alcohol (*c* 4.49). When one drop of a solution of hydrogen bromide in benzyl alcohol was added, the rotation fell to +22° in 2 hours. The rotation of benzyl β-D-ribofuranoside tribenzoate[1] in benzyl alcohol (*c* 4.24) is 0.0 ± 0.5° (*l* 0.5 dm.). The remainder of the sirup (6.46 g.) was dissolved in 40 ml. of ethyl acetate and 5 g. of previously activated and washed palladium–charcoal[20] added to the solution. The mixture was shaken at room temperature and pressure with hydrogen for 3 hours, filtered and concentrated to a sirup which, from 25 ml. of absolute ether, gave 1.07 g. (21%) of material melting at 141–143° either alone or in admixture with 3,5-di-*O*-benzoyl-1,2-*O*-(1-hydroxybenzylidene)-α-D-ribose prepared in (a) above. The material remaining in the mother liquor gave, from carbon tetrachloride solution, 2.59 g. (52%) of 2,3,5-tri-*O*-benzoyl-β-D-ribose melting at 103–107°.

Behavior of 3,5-Di-*O*-benzoyl-1,2-*O*-(1-hydroxybenzylidene)-α-D-ribose (II) with Dilute Hydrobromic Acid and Dilute Ammonia.—Twenty-five milliliters of 18:7 (v./v.) dioxane–water containing 0.5114 g. of the ortho acid derivative showed a specific rotation of +74°. The addition of 0.016 ml. of *ca.* 41% hydrobromic acid failed to change this value over a period of 2 months. A similar solution containing 0.5013 g. of the ortho compound showed a specific rotation of +73°; when 2 drops of concentrated aqueous ammonia was added the rotation fell to +66.7° in 2 hours. 2,3,5-Tri-*O*-benzoyl-β-D-ribose (IV) showed a rotation of +67.3° in 18:7 dioxane–water (*c* 1.01); 1.3 hours after the addition of 2 drops of concentrated aqueous ammonia the rotation had become +67.6°.

2,3,5-Tri-*O*-benzoyl-β-D-ribose (IV) from 3,5-Di-*O*-benzoyl-1,2-*O*-(1-hydroxybenzylidene)-α-D-ribose (II).—One gram of the pure orthobenzoic acid derivative was dissolved in a mixture of 10 ml. of pyridine and 2 ml. of water. After 31.5 hours at room temperature the solution was cooled to 0°, diluted with 6 ml. of water and seeded with 2,3,5-tri-*O*-benzoyl-β-D-ribose containing pyridine of crystallization.[1] As crystallization proceeded 4 ml. more water was added. Freed of pyridine by drying at 40° *in vacuo* over phosphorus pentoxide, the product weighed 0.89 g. Recrystallized from a mixture of 2 ml. of absolute alcohol and 3.6 ml. of pentane the substance (0.65 g., 65%) was obtained in solvent-free form melting at 102–104°. Recrystallized from 2 parts of carbon tetrachloride the fine needles (0.60 g.) rotated +68.7° (*c* 2.05, U.S.P. $CHCl_3$) and melted at 106–108° either alone or in admixture with authentic 2,3,5-tri-*O*-benzoyl-β-D-ribose.

3,5-Di-*O*-benzoyl-D-ribofuranosyl Bromide (VII).—3,5-Di-*O*-benzoyl-1,2-*O*-(1-hydroxybenzylidene)-α-D-ribose (II, 0.5489 g.) in methylene chloride (15.0 ml. total volume) showed an observed rotation of +4.66° in a 1.5-dm. tube. A gentle stream of hydrogen bromide was passed over the surface of the solution in the tube for 30 seconds and then, after thorough mixing, the clear solution showed the following observed rotations: +2.79° (1.5 min.), +4.63° (2.8 min.), +5.32° (max., 5.7 min.[21]), +4.98° (10 min.). The reaction mixture was concentrated *in vacuo* at 0° to give a semi-crystalline mass which, from 1 ml. of absolute ether and 1.1 ml. of pentane at 0°, afforded 0.497 g. (99%) of a bromide which melted with rapid decomposition at 88–91° (rate of heating 4°/min., sample introduced at 85°). Recrystallized from 11 ml. of 3:5:3 methylene chloride–ether–pentane at −5° the product (0.260 g.) melted with decomposition at 104–105° (rate of heating 3°/min., sample introduced at 100°). In absolute chloroform (*c* 0.47) the bromide mutarotated from +96° (3 min.) to +27° (60 min., constant).[22]

Anal. Calcd. for $C_{19}H_{17}O_6Br$: C, 54.17; H, 4.07; Br, 18.97. Found: C, 55.10; H, 4.13; Br, 17.70.

The above analytical values fall between those calculated for the bromide and those calculated for its presumed hydrolysis product, 3,5-di-*O*-benzoyl-D-ribose ($C_{19}H_{18}O_7$: C, 63.68; H, 5.07)—a not unexpected result in view of the lability of the former substance.

Amorphous 3,5-Di-*O*-benzoyl-D-ribose (VI) and its Conversion to Erythritol Tetrabenzoate (XI).—3,5-Di-*O*-benzoyl-D-ribofuranosyl bromide (VII, 1.00 g.) was hydrolyzed in a cooled mixture of 10 ml. of acetone, 1 ml. of water and 1 g. of silver carbonate. After being stirred for 40 minutes, the mixture was filtered, the filtrate dried with sodium sulfate and then concentrated *in vacuo* (25° bath) to a clear, colorless sirup. Attempts to crystallize this product failed. A sample (0.3840 g.) was dissolved in a little glacial acetic acid, the solution treated with 50.0 ml. of 0.0568 *N* lead tetraacetate in glacial acetic acid and the reaction mixture diluted to 100.0 ml. with the same solvent. After 1, 4 and 22 hours analysis of aliquots by the method of Hockett and McClenahan[23] showed the consumption of 0.78 mole of oxidant per mole of compound. No formic acid was detected.[24] The remainder of the oxidation mixture (39.5 ml.) was poured into a cold mixture of 200 ml. of methylene chloride, 200 ml. of water, 40 g. of sodium acetate, 2.3 g. of potassium iodide and 6 ml. of 0.1 *N* sodium thiosulfate. After thor-

---

(20) R. Mozingo, *Org. Syntheses*, **26**, 77 (1946); method C.

(21) A similar run was halted at its maximum rotation by pouring the mixture into a mixture of acetone, water and silver carbonate. When neutralization was complete the solids were filtered off and the filtrate concentrated to a mixture of crystals and sirup. Repeated extraction of this material with pentane afforded a quantity of benzoic acid corresponding to 69% of theory. The acid melted at 118–121° and did not depress the melting point of authentic benzoic acid.

(22) While fully acylated glycosyl halides do not mutarotate when dissolved in inert solvents, P. Brigl [*Hoppe-Seyler's Z. physiol. Chem.*, **116**, 1 (1921)] found that 3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl chloride mutarotates in acetone solution. R. U. Lemieux and G. Huber [*Can. J. Chem.*, **31**, 1040 (1953)] have recently shown that this mutarotation is due to anomerization.

(23) R. C. Hockett and W. S. McClenahan, THIS JOURNAL, **61**, 1667 (1939).

(24) The method which W. Poethke [*Pharm. Zentralhalle*, **86**, 357 (1947)] developed for the determination of formic acid in acetic acid was adapted for the present purpose. As mentioned earlier, possibly the initial cleavage of the 3,5-di-*O*-benzoyl-D-ribose (VI) between carbons 1 and 2 formed a 2,4-di-*O*-benzoyl-3-*O*-formyl-D-erythrose (IX) which did not readily hydrolyze to formic acid. However, the second stage in the lead tetraacetate oxidation of methyl α-D-mannopyranoside (*i.e.*, cleavage between carbons originally numbered 3 and 4 after cyclic acetal formation between carbons 3 and 6) should give rise to a similar formic acid ester and in this case it was found that when 1.63 molar equivalents of oxidant had been consumed 0.63 molar equivalent of formic acid was liberated. Of course, the product from the oxidation of 3,5-di-*O*-benzoyl-D-ribose would bear a secondary formyl group, while that from methyl α-D-mannopyranoside would have a primary formyl radical.

ough shaking, the organic layer was washed with aqueous sodium bicarbonate, dried with sodium sulfate and concentrated *in vacuo* to a sirup. Dissolved in 8 ml. of absolute alcohol to which Raney nickel had been added, this material was hydrogenated at 2250 p.s.i. for 19 hours at room temperature. After removal of the catalyst and concentration *in vacuo* there was obtained a sirup which gave a negative Fehling test. The acyl groups were removed catalytically with barium methoxide in the usual manner and the product benzoylated with benzoyl chloride in pyridine. The product, worked up in the usual manner, crystallized spontaneously from ether; 0.0926 g. (41%), m.p. 181–186°. Recrystallized from 1:1 benzene–hexane and then from 1:1 methylene chloride–absolute alcohol the product showed no rotation in chloroform (*c* 1.65, 4 dm.) and melted at 189–190° alone or in admixture with authentic erythritol tetrabenzoate.

1,2-Di-*O*-acetyl-3,5-di-*O*-benzoyl-D-ribose (V). (a) From 3,5-Di-*O*-benzoyl-1,2-*O*-(1-hydroxybenzylidene)-α-D-ribose (II).—A solution of 0.45 g. of fused zinc chloride in 8 ml. of acetic anhydride was cooled in an ice-bath and 1.0 g. of 3,5-di-*O*-benzoyl-1,2-*O*-(1-hydroxybenzylidene)-α-D-ribose (II) added in portions over a period of 6 minutes. After standing at 5° for 20 hours, the reaction mixture was poured into 60 ml. of water. After several hours the somewhat brittle mass thus precipitated was separated and dissolved in 3 ml. of warm absolute alcohol from which it gave 0.52 g. (54%) of sheaves of heavy needles melting at 125–127° and rotating −3.2° in chloroform (*c* 1.49). Recrystallization from 11 parts of absolute alcohol afforded pure 1,2-di-*O*-acetyl-3,5-di-*O*-benzoyl-D-ribose melting at 127–128° and rotating −3° in chloroform (*c* 0.82).

Anal. Calcd. for $C_{23}H_{22}O_9$: C, 62.44; H, 5.01. Found: C, 62.52; H, 5.05.

(b) **From 3,5-Di-*O*-benzoyl-D-ribofuranosyl Bromide (VII).**—A solution of 0.1024 g. of the bromide, prepared as described above, in 2.00 ml. of acetic anhydride was observed in a 0.5-dm. tube to mutarotate rapidly: +0.53° (2.0 min.), +0.91° (3 min.), +1.12° (5.4 and 13.6 min.). After 15 minutes a small quantity of powdered, fused zinc chloride was added and the rotation observed to change almost instantly to +0.31° (1.5 and 5.3 min.). Nine minutes later the reaction mixture was poured on ice; the mass thus precipitated gave, from 0.5 ml. of absolute alcohol, 0.0642 g. (60%) of material melting at 126–127°. Mixed with 1,2-di-*O*-acetyl-3,5-di-*O*-benzoyl-D-ribose prepared earlier it melted at 125–127°.

3,5-Di-*O*-benzoyl-1,2-*O*-(1-hydroxyethylidene)-α-D-ribose (VIII). (a) From 3,5-Di-*O*-benzoyl-1,2-*O*-(1-hydroxybenzylidene)-α-D-ribose (II).—A solution of 1.03 g. of 3,5-di-*O*-benzoyl-1,2-*O*-(1-hydroxybenzylidene)-α-D-ribose in a mixture of 5 ml. of methylene chloride and 0.3 ml. of acetic anhydride was treated with 7 ml. of a solution of hydrogen bromide in glacial acetic acid (32% HBr). After 16 minutes at room temperature the reaction mixture was poured on ice with methylene chloride. The organic layer was washed with water and aqueous sodium bicarbonate, hydrolysis taking place spontaneously at this stage. Moisture was removed with sodium sulfate and the solution concentrated *in vacuo* (30° bath) to a clear sirup which, from a mixture of 5 ml. of absolute ether and *ca.* 2.5 ml. of pentane gave crystals melting at 92–97°. Recrystallized from 10 ml. of warm ether the product (0.132 g., 15%) melted at 124–125°. After another recrystallization from ether the material melted at 129–130° and showed a rotation in chloroform of +66.4° (*c* 1.26). Further recrystallization failed to change these values.

Anal. Calcd. for $C_{21}H_{20}O_8$: C, 62.99; H, 5.04. Found: C, 62.92; H, 4.87.

A sample (0.1217 g.) of the compound in 7.2 ml. of dioxane was diluted to 10.0 ml. with water. In a 1.5-dm. tube at 20° the solution showed an observed rotation of +1.13°. Sixteen hours after adding 1 drop of 41% hydrobromic acid the observed rotation was +1.03°. When 0.15 ml. of pyridine was added the observed rotation changed more rapidly: +0.99° (3 min.), +0.79° (7 hr.), +0.48° (24 hr.), +0.40° (31 hr.), +0.32° (49 hr., constant).

(b) **From 1,2-Di-*O*-acetyl-3,5-di-*O*-benzoyl-D-ribose (V).**—A solution of 1.00 g. of 1,2-di-*O*-acetyl-3,5-di-*O*-benzoyl-D-ribose in 10.0 ml. of ethylene chloride was observed in a 1.5-dm. tube to rotate −0.37°. The addition of 0.24 ml. of acetic anhydride changed the observed reading to −0.36°. When 9.7 ml. of a solution of hydrogen bromide in glacial acetic acid (32% HBr) was added the observed rotation changed rapidly: −1.40° (1.0 min.), −0.05° (1.4 min.), +1.21° (3.5 min.), +1.24° (12 min.). After 18 minutes the reaction mixture was poured in ice water with methylene chloride. Washing with aqueous sodium bicarbonate and then with water completed the hydrolysis of the bromide. The solution was dried with sodium sulfate and concentrated *in vacuo* (35° bath) to a thick sirup, which, from 2 ml. of ether, afforded 0.188 g. of crystals melting at 115–118°. A second crop of 0.063 g. melting at 115–119° raised the total yield to 28%. Recrystallized from 1:1:1 methylene chloride–ether–pentane and then from 2:1 ether–pentane the combined crops afforded 0.084 g. of needles rotating +68.2° in chloroform (*c* 0.33) and melting at 127–128° either alone or in admixture with the product obtained in (a) above. Recrystallized from ether the material melted at 128–129°, but a second recrystallization from methylene chloride–pentane gave a product which showed a double melting point: 105–106°, 127–128°.

1-*O*-Acetyl-2,3,5-tri-*O*-benzoyl-D-ribose from β-D-Ribofuranose Tetrabenzoate.—Pure β-D-ribofuranose tetrabenzoate[1] (0.4175 g.) was dissolved in 4.0 ml. of acetic anhydride and the solution treated at 20° with 1 ml. of a solution of 2.0 g. of fused zinc chloride in 10 ml. of acetic anhydride. After mutarotation had ceased (4 hr.) the reaction mixture was poured on ice. The gum which precipitated gave from absolute alcohol 0.2084 g. (56%) of crystalline product melting at 128–129°. One recrystallization from 5 ml. of absolute ethanol afforded hexagonal micaceous plates melting at 129–130° either alone or in admixture with authentic 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-D-ribose.[1]

Acknowledgments.—We wish to thank Dr. William R. Nes, Mrs. Iris J. Siewers and Mrs. Anne H. Wright for measurement and interpretation of absorption spectra. We are also indebted to Mr. Harry W. Diehl for assistance in one of the preparations and to the Institute's Microanalytical Laboratory, under the direction of Dr. William C. Alford, for combustion analyses.

BETHESDA 14, MARYLAND